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GEOFFREY WOODARD, PH.D.

WOODARD RESEARCH CORPORATION

HERNDON, VIRCINIA

TESTING OF ANTIRADIATION AGENTS IN MONKEYS, AS AMENDED

DA-49-193-MD-2458

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ABSTRACT

1. Preparing Instituition: Woodard Research Corporation
2. Title of Report: Annual Progress Report
   Testing of Antiradiation Agents in Monkeys, as amended
3. Principle Investigator: Geoffrey Woodard
4. Number of Pages: 3
5. Contract Number: DA 49-193-MD-2458
6. Supported by: U. S Army Medical Research and Development Command
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~~Several~~ compounds which have been shown to be protective against ionizing radiation ~~have been~~ were studied with respect to the evaluation of their safety when administered to rhesus monkeys. Various parameters such as body weight gain, hemograms, blood and urine analyses and histopathological observations ~~have been~~ were employed. ~~Additional work, such as~~ a teratogenic evaluation in rats and a blood picture study in splenectonized rabbits, which are described, is now being carried out ~~as per an amendment to the original contract~~.

Key Words: Testing, Antiradiation Agents, Monkeys

Note: Copies of this report are filed with the Defense Documentation Center, Cameron Station, Alexandria, Virginia 22314 and may be obtained from that agency by qualified investigators working under government contract.

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REPORT

For purposes of this report, the work done during the previous contract period may be divided as follows:

1. Safety evaluation of mercaptoethylamine by repeated oral administration to monkeys
2. Acute intravenous toxicity of some radioprotective agents in monkeys
3. Teratogenic evaluation of mercaptoethylamine in monkeys
4. A study of leukopenia in splenectonized rabbits following administration of various aminothiol compounds

These last two sections are provided for in the amendment to the contract

1. Safety Evaluation of Mercaptoethylamine by Repeated Oral Administration to Monkeys - Two groups of rhesus monkeys (Macaca mulatto) have been receiving mercaptoethylamine by stomach tube daily, seven days per week for a period of 32 weeks. It is anticipated that this compound will be administered for a total period of 52 weeks. One group of animals has received a daily dosage of 20 mg/kg while the other group has received an increasing dose which is presently at 62 mg/kg/day. A group of control animals, receiving vehicle by the same route are being studied concurrently.

The following parameters are being observed in determining the effects of mercaptoethylamine on these monkeys:

Body weight gain
Food consumption
Hemograms (WBC, RBC, PCV, hemoglobin, plasma hemoglobin)
Blood urea nitrogen
Serum alkaline phosphatase
Serum glutamic oxalacetic transaminase
Serum glutamic pyruvic transaminase
Serum electrophoresis
Sulfhydryl levels in blood and urine
Disulfide levels in blood and urine
Kynurenine levels in urine
Sulfate levels in urine
Qualitative urinalyses
Gross and microscopic pathology

To date, results of these tests show no deviation from control figures which could be attributed to compound administration, with the exception of a general decrease in body weight gain observed for those animals receiving mercaptoethylamine at the increasing or flexible dose.

2. Acute Intravenous Toxicity of some Radioprotective Agents in Monkeys - Three coded chemical compounds, found to protect against ionizing radiation were studied for their acute intravenous toxicity to rhesus monkeys The compounds were administered daily for a period of, at least five days, during which time, a number of measurements and clinical tests were carried out. At this time, the animals were sacrificed and tissues were subjected to gross and microscopic examination.

3. Teratogenic Evaluation of Mercaptoethylamine in Rats - A reproduction study that is required by the Food and Drug Administration is being initiated on rats which will receive mercaptoethylamine in their diet at two levels plus controls. After the animals have received their respective diets for approximately 70 days, the males and females from each group will be paired to mate for a period of 10 days. All offspring from this mating will be closely examined at birth. Examination will include the following observations:

Date of birth
Number of live offspring
Number of stillbirths
Physical condition of the offspring
Physical condition of the stillbirths
Mean birth weight

Surviving offspring will again be weighed and closely examined at weaning, then sacrificed and subjected to gross necropsy.

Parent females will then be remated, this time with a different male and the procedures for litter No. 1 will be repeated. After necropsy of the second litters at weaning, the parent rats also will be sacrificed, but without autopsies, unless indicated.

4. Study of Leukopenia in Splenectonized Rabbits Following Administration of Various Aminothiol Compounds - Since it has been found that penicillamine and thiouracil produce leukopenia in laboratory animals, an experiment has been initiated to study the effects of these and other aminothiols such as mercaptoethylamine on the white blood cells of splenectonized rabbits. Results of this experiment will indicate whether mercaptoethylamine produces leukopenia in rabbits at a rate comparable to that of penicillamine or thiouracil. Also, this experiment could then be repeated, as a screening test, with additional candidate antiradiation compounds to study their ability to produce leukopenia.

Each group of animals is to be given their respective compound in the diet, seven days per week, with daily physical observations. Weekly parameters to be studied include:

Body weight gain
Food Consumption
Hematocrit
Total and differential white cell counts
Hemoglobin (initially and terminally)

At termination, all animals will be sacrificed and tissues will be subjected to gross and microscopic examination.

Geoffrey Woodard

Geoffrey Woodard, Ph.D.
Pharmacologist

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DISTRIBUTION LIST

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